

PE 1/31/02

### FORM 6-K

SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

Pursuant to Rule 13a-16 or 15d-16 of the Securities Exchange Act of 1934

Report of Foreign Issuer for the period of 1st July 2002 to 31st July 2002



**British Biotech plc** 

Thames Court Watlington Road Oxford OX4 6LY England **PROCESSED** 

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THOMSON FINANCIAL

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Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20F or Form 40F.

Form 20F	$\mathbf{X}^{-r}$	Form 40F

Indicate by check mark whether the registrant by furnishing the information contained in this Form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes	No	X

If "Yes" is marked, indicate below the file number assigned to the registrant in connection with Rule 12g3-2(b): 82 - \_\_\_\_

### **SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

### **BRITISH BIOTECH PLC**

(Registrant)

By: 1. 4. Date: 12th August 2002

Name: Tony Weir

Title: Finance Director

# News Release

**British Biotech** 

5 July 2002

# British Biotech plc: Preliminary financial results for the year ended 30 April 2002

British Biotech plc (LSE: BBG, Nasdaq: BBIOY) today announced its preliminary financial results for the year ended 30 April 2002.

### **Business highlights**

- BB-10901
  - Phase I/II study under way in relapsed/refractory small cell lung cancer (weekly dosing)
  - CTX granted for UK Phase I study
- E21R
  - Phase II study stopped in acute myeloid leukaemia
  - Phase II study continuing in chronic myelomonocytic leukaemia
  - Orphan drug designation for juvenile myelomonocytic leukaemia (EU)
- BB-10153
  - Successful manufacturing campaign
  - Phase II proof-of-principle study in acute myocardial infarction to start July 2002
- Product Portfolio expanded with the grant of European development and commercialisation rights to MG98 from MethylGene Inc.
- Antibiotic Programme
  - BB-83698 to start Phase I by October 2002
  - Nine presentations at 41<sup>st</sup> ICAAC (December 2001); eight presentations accepted for 42<sup>nd</sup> ICAAC (September 2002)
- Biodefence research agreement with UK Government's Defence Science and Technology Laboratory
- Batimastat BiodivYsio<sup>®</sup> stent
  - Development suspended
- Final stage of restructuring completed with the sale of non-core assets to OSI Pharmaceuticals, Inc., and the successful recruitment of experienced pharmaceutical industry executives into key operational roles

## Financial highlights

- Loss for the year reduced to £16.9 million (2001: £23.4 million)
- Annual cash burn of £14.6 million (2001: £10.7 million)
- Cash and short term investments of £50.4 million at 30 April 2002

Commenting on the year's results, Dr Elliot Goldstein, Chief Executive Officer of British Biotech, said: "In a challenging economic environment for biotechnology companies, British Biotech continues to make progress. With products in the clinic, strong development capabilities and cash, British Biotech is well placed for strategic initiatives in Europe and North America that will strengthen our platform for growth and the creation of shareholder value."

### For further information, please contact:

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This news release contains forward-looking statements that reflect the Company's current expectation regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the success of the Company's research strategy, the applicability of the discoveries made therein, the successful and timely completion of clinical studies and the uncertainties related to the regulatory process.

### British Biotech plc ("British Biotech")

### Preliminary results for the year ended 30 April 2002

### 1. Business Review

### **Company Strategy**

British Biotech's strategy is to create long-term value for shareholders by building a product portfolio of innovative medicines, targeted mainly at cancer but based on a variety of technologies, and to bring these to market as expeditiously as possible. The Company has retained commercialisation rights, in various territories, to all of the products in the portfolio and value will be created as the Company generates data from later-stage clinical trials over the next three years.

The Company adopts a highly rigorous approach to its development activities. Should any product fail to meet its clinical endpoints, development will cease and it will be dropped from the portfolio. The portfolio will continue to be expanded by drug development candidates emerging from in-house research and by the acquisition of rights to products discovered by other companies. The Company is actively seeking further collaborations where it can apply its development capabilities to create additional value. Additionally, the Board is looking at ways in which the Company can enhance shareholder value by combining its own portfolio, development capabilities and cash with those of other businesses in Europe and North America.

### Restructuring

In August 2001 British Biotech completed the final stage in its restructuring programme, enabling it to intensify its focus on drug development, add to cash resources, and reduce significantly its fixed infrastructure costs.

Under an agreement with OSI Pharmaceuticals, Inc., (Nasdaq: OSIP), British Biotech transferred part of its pre-clinical research facilities to OSI, including 59 employees, leases on two properties, and fixed assets with a net book value of £5.0 million. British Biotech received £8.7 million in cash and reduced the Company's fixed infrastructure costs by £6.0 million per annum. Following the restructuring, British Biotech had 87 full-time employees at 30 April 2002.

### People

In line with its focus on products, British Biotech has sought to strengthen its development capabilities, and has been successful in recruiting experienced executives from established pharmaceutical companies such as Pfizer, Glaxo SmithKline, Novartis and Johnson & Johnson to key managerial and operational roles in clinical development, business development and regulatory affairs. The Company has also expanded its chemistry and pharmaceutical development functions to support its research and development of novel antibiotics and for its collaborative research with Serono into anti-inflammatory treatments.

# 6

#### **Product Portfolio**

British Biotech's Product Portfolio currently comprises four drugs in clinical development and one product in late-stage pre-clinical development.

Product/ Partner	Indications	Clinical Development Status	Commercial Rights	Next Milestones
BB-10901 ImmunoGen Inc. (USA)	Small cell lung cancer Neuroendocrine tumours Carcinoid	Currently in Phase I to establish maximum tolerated dose (weekly dosing)  CTX granted for UK Phase I study (more frequent dosing)	■Europe, Japan	Start Phase I (UK) Q3 2002 Start Phase II Q4 2002
E21R BresaGen Ltd (Australia)	■CMML ■JMML (EU orphan status designation)	<ul> <li>AML Phase II study stopped</li> <li>CMML pilot Phase II study ongoing</li> <li>JMML development under discussion with regulators and external experts</li> </ul>	■ Global	Start JMML development Q3 2002 CMML Phase II results Q4 2003
MG98 MethylGene Inc. (Canada)	Gastric cancer AML/MDS Other cancers involving hyper- methylation	AML/MDS Phase I dose and schedule optimising study study ongoing     Head/neck cancer, renal carcinoma Phase II studies – recruitment closed	■ Europe	Start European studies Q4 2002
BB-10153	<ul> <li>Acute myocardial infarction</li> <li>Stroke</li> <li>Peripheral arterial occlusion</li> </ul>	Phase II in AMI to start in July (in collaboration with TIMI Study Group)	■Global	Phase II data Q2 2003
BB-83698	Community-acquired pneumonia (hospitalised patients)	■ Pre-clinical	■ Global	Start Phase I i.v. study October 2002

**BB-10901** – BB-10901 is being developed jointly by British Biotech and the US biotechnology company ImmunoGen, Inc (Nasdaq: IMGN). It is an immunoconjugate of the cytotoxic maytansinoid drug, DM1, with the humanized monoclonal antibody huN901 and is designed to selectively kill certain types of cancer cells including those found in small cell lung cancer (SCLC). In pre-clinical studies, and in contrast to current cytotoxic therapy, BB-10901 completely eradicated SCLC tumours.

In May 2001, British Biotech began a combined Phase I/II clinical study at two centres in the USA to evaluate the safety, tolerability and biological activity of weekly infusions of BB-10901. Initial Phase I data were presented at the 2002 meeting of the American Society of Clinical Oncology. These showed the drug was well tolerated, with no dose-limiting toxicity, at weekly doses up to and including 60mg/m<sup>2</sup>. Recruitment of patients at the sixth dose level of 75mg/m<sup>2</sup> is continuing. Once the maximum tolerated dose has been established, an additional 29 patients will be treated at that dose in the Phase II portion of the study. This progression to Phase II is expected in Q4 2002.

7

In April 2002, the UK's Medicines Control Agency granted a Clinical Trials Exemption (CTX) to British Biotech for a Phase I study of BB-10901 to investigate the safety of the drug when administered on a more frequent dosing regime. This study is expected to start shortly; further details will be published when the study begins.

British Biotech has commercialisation rights for BB-10901 in Europe and Japan. ImmunoGen retained rights for America and the rest of the world.

**E21R** – E21R is a modified form of granulocyte-macrophage colony-stimulating factor (GM-CSF) being developed in collaboration with the Australian biotechnology company, BresaGen Ltd. (ASX: BGN).

BresaGen completed Phase I clinical testing of E21R in 2000. In August 2001, British Biotech started a Phase II study to investigate E21R's efficacy, safety, tolerability and pharmacokinetics in patients with acute myeloid leukaemia (AML). This study has now been stopped since new pre-clinical data have failed to support the previous high incidence of apoptosis (cell killing) in AML. Further pre-clinical studies are under way to assess the rationale for development of E21R in AML.

These new pre-clinical data do not call into question the rationale for development of E21R in chronic myelomonocytic leukaemia (CMML) and juvenile myelomonocytic leukaemia (JMML). BresaGen is continuing to recruit patients to a pilot Phase II study in CMML. Also, in March 2002, the European Commission designated E21R as having orphan drug status for the treatment of JMML, a rare and deadly disease affecting very young children. The orphan designation is based on the rare and serious nature of the disease, the lack of satisfactory therapy and the product's potential to have significant therapeutic benefit. Discussions with regulators and clinical experts on the appropriate clinical development programme in JMML are ongoing.

Under its collaboration with BresaGen, British Biotech has exclusive world-wide rights to commercialise E21R for all indications.

MG98 – In February 2002, British Biotech was granted European development and commercialisation rights for MG98, a novel second-generation antisense compound discovered by MethylGene Inc., a privately-held Canadian company. MG98 is designed to inhibit the expression of DNA methyltransferase (DNMT), an enzyme implicated in uncontrolled tumour growth. MethylGene granted North American development and commercialisation rights for MG98 to MGI PHARMA in August 2000.

During the Phase I trials of MG98, one patient receiving MG98 under a twice-weekly regimen experienced a sustained (>6 months) objective partial response (>70% reduction in the sum of bidimensional products of measurable lesions). This regimen was well tolerated in the all-comer solid tumour population examined, and this regimen was chosen for use in the first Phase II trials.

Two such North American Phase II studies investigating twice-weekly administration of MG98 monotherapy in patients with head and neck cancer (conducted by MethylGene) and renal cell carcinoma (sponsored by MethylGene in collaboration with the National Cancer Institute of Canada Clinical Trials Group) have closed recruitment. In these studies MG98, at the doses and twice-weekly schedule tested, did not demonstrate objective clinical responses as defined by the

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A Phase I trial investigating multiple doses and schedules in patients with advanced myelodysplasia and acute myeloid leukaemia, in order to optimise dose and schedule for additional trials, was initiated by MGI PHARMA in January 2002 and continues to recruit patients. British Biotech plans to initiate in Q4 2002 a further Phase I study to investigate the safety and tolerability of a continuous infusion regimen in patients with solid tumours such as gastric adenocarcinoma. Results from these Phase I studies will form the basis of any future Phase II programme.

**BB-10153** – BB-10153 is a novel thrombolytic (clot-busting) agent discovered by British Biotech. It is an engineered form of human plasminogen, modified so that it is activated to plasmin by thrombin, which is only produced at the site of fresh blood clots, rather than by the body's natural plasminogen activators such as tPA. Pre-clinical testing showed that BB-10153 only dissolves recently-formed or still-forming clots. A Phase I study, at doses up to 4.8mg/kg, demonstrated the drug to be safe in healthy volunteers.

During the year in review, GMP production of material for a Phase II study was completed and in March 2002, the US Food & Drug Administration gave the go-ahead to test BB-10153 in heart attack patients. Supplies of the drug and the necessary approvals are now in place to begin this study, which will be conducted by the US-based Thrombolysis in Myocardial Infarction (TIMI) Study Group. The study will test the ability of BB-10153, given at doses between 1 and 5mg/kg, to dissolve clots and restore blood flow in the coronary arteries of heart attack patients. The study will also evaluate the safety of treatment with BB-10153, especially with respect to bleeding.

Data from the study are expected to be available in mid-2003 and will be used to attract potential collaborators for continued development and commercialisation of this product.

**BB-83698** – Targeted at community-acquired pneumonia (hospitalised patients), BB-83698 is the lead peptide deformylase inhibitor from British Biotech's Antibiotic Programme. In completed pre-clinical studies BB-83698 has shown high potency against a range of gram positive bacteria, including several drug-resistant strains. The toxicology studies necessary to allow human dosing have been carried out and final analysis of data is nearing completion. A Phase I clinical study in healthy volunteers, to determine the safety and pharmacokinetics of single doses of an intravenous formulation, is expected to begin in October 2002.

### **Other Product Development Programmes**

Batimastat Biodiv Ysio® stent – Clinical development of this product was suspended in March 2002 pending further review of data from the BRILLIANT I clinical trial. BRILLIANT I is a 150 patient multi-centre open clinical trial, recruitment for which was completed in November 2001. Six-month angiographic and clinical follow-up on an initial group of patients from this trial indicated that the product was unlikely to show the benefit that was evident in the pre-clinical studies. Additional patient data is being collected and analysed, after which a final decision will be made to continue or end this programme.

### Research

Antibiotic Programme – British Biotech's research into antibiotics is founded on the Company's strong intellectual property position in bacterial metalloenzyme inhibitors. The programme has produced several lead compounds in research and pre-clinical development, with

9

In December 2001 Company researchers and external scientific collaborators presented details of this research at the 41<sup>st</sup> Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). The presentations covered the *in vitro* and *in vivo* efficacy of British Biotech's peptide deformylase inhibitor compounds against a variety of drug-resistant pathogens; research into the antibiotic activity and characterisation of inhibitors of the 'LpxC' metalloenzyme; and the use of bio-informatics in the Company's antibiotic drug discovery programme.

British Biotech will be giving a further update on its Antibiotic Programme at the 42<sup>nd</sup> ICAAC (San Diego, 27-30 September 2002), where eight presentations have been accepted.

Serono Collaboration – The research collaboration formed in October 2000 between British Biotech and Serono SA (SWX: SEO, NYSE: SRA) to identify new treatments for serious inflammatory diseases, particularly multiple sclerosis, has made good progress. The two companies have completed screening of British Biotech's compound library against pathologically relevant metalloenzyme targets, and identified selective inhibitors active against three enzyme targets involved in inflammatory indications.

Cancer Programme – In February 2002, British Biotech was granted an exclusive one year option, renewable for a second year, for European development and commercialisation rights of compounds from MethylGene's research programme into small molecule inhibitors of DNA methyltransferase.

**Biodefence Research Initiative** – As part of the UK Government's biodefence initiative, the Company has entered into an agreement with the Defence, Science and Technology Laboratory (DSTL) of Porton Down to investigate the utility of selected British Biotech metalloenzyme inhibitors against anthrax lethal toxin and botulin toxin.

### Other matters

The Company has noted the recent press comment regarding Class Law, an English firm of solicitors, and putative claims against the Company in respect of events more than four years ago. The Company understands that Class Law has been attempting to solicit interest in such claims since at least February 2001 and since such time has also been regularly suggesting that proceedings against the Company are imminent. Such proceedings have not been forthcoming. The Company has considered the nature of Class Law's putative, but unspecified, claims with its legal advisers and believes them to be without merit or foundation.

## 2. Objectives

The principal objectives for the current financial year are:

- Meet the product development milestones detailed in the table above;
- Add at least one new product to the portfolio through collaboration;
- Form a collaboration on the Antibiotic Programme;
- Explore strategic growth opportunities, in particular mergers or acquisitions.

### 3. Financial review

#### Profit and loss account

The loss for the year ended 30 April 2002 decreased to £16.9 million (2001: £23.4 million) due to reduced levels of expenditure and the profit arising from the restructuring and the transfer, in August 2001, of certain pre-clinical facilities to OSI Pharmaceuticals, Inc. Research and development tax credits of £1.6 million were recognised in the year (2001: £nil), as the Company believes it has satisfied the requirements of the Finance Act 2000 for the year ended 30 April 2002.

Turnover in the year amounted to £1.5 million (2001: £1.6 million). The turnover resulted principally from the agreement with Serono to research, develop and commercialise metalloenzyme inhibitors in serious inflammatory disease, with £1.4 million (2001: £1.3 million) of the £3.3 million received from Serono in November 2000 recognised as income in the year. Research and development expenditure for the year was £2.7 million lower at £21.0 million (2001: £23.7 million) due to lower infrastructure costs following the restructuring in August 2001.

Administrative expenses for the year were lower at £3.8 million (2001: £4.0million) including a charge of £0.2 million (2001: £nil) in respect of share options. The lower expenditure is due to savings from the restructuring implemented in August 2001. Profit of £2.5 million on the disposal of fixed assets arose on the restructuring from the transfer of certain pre-clinical facilities to OSI. The amortisation of intangible fixed assets was £0.2 million (2002: £0.1 million).

Interest receivable was £2.8 million (2001: £3.8 million) with the reduction due to lower interest rates and lower average cash balances during the year. Amounts written off investments in the year were £ 0.3 million (2001: £0.8 million).

### Cash flow

The reduction in cash and short term investment balances during the year was £14.6 million (2001: £10.7 million) comprising cash utilised by operations of £14.3 million (2001: £10.3 million) and financing repayments of £0.3 million (2001: £0.4 million). The cash utilised by operations benefited from the receipt of £8.7 million from OSI in 2002 and from the proceeds of the sale and leaseback of the office facility of £11.2 million in 2001. Excluding these amounts, the cash utilised by operations was £23.0 million (2001: £21.5 million). The increase was due to lower interest received of £1.3 million, increased capital expenditure of £0.8 million on the fitout of laboratories and offices following the OSI transaction and additional expenditure on the Product Portfolio of £2.6 million. These were offset by lower infrastructure costs in the second half of the year of £3.0 million following the restructuring. These lower infrastructure costs represent a permanent annualised cost saving of some £6 million.

Cash and short-term investments at 30 April 2002 were £50.4 million, compared with £65 million at 30 April 2001.

# Unaudited consolidated profit and loss account for the year ended 30 April 2002

	2002 £000	2001 £000
Turnover	1,450	1,588
Research and development expenditure Administrative expenses	(20,955) (3,759)	(23,724) (3,997)
Operating loss	(23,264)	(26,133)
Profit on disposal of fixed assets Interest receivable Amount written off investments Interest payable	2,505 2,820 (324) (278)	3,778 (799) (329)
Loss on ordinary activities before taxation	(18,541)	(23,483)
Taxation	1,608	130
Loss for the financial year transferred to reserves	(16,933)	(23,353)
Loss per share (basic and diluted) (Note 3)	(2.5)p	(3.5)p

# Unaudited statement of total recognised gains and losses for the year ended 30 April 2002

	2002	2001
	£000	£000
Consolidated loss for the financial year Translation of overseas subsidiary financial statements	(16,933) 3	(23,353) 25
Total recognised losses relating to the year	(16,930)	(23,328)

# Unaudited consolidated balance sheet as at 30 April 2002

		2001
	2002	Restated
	£000	(Note 4)
		£000
Fixed assets		
Intangible assets	2,288	1,090
Tangible assets	7,996	13,053
Investments	1,906	824
	12,190	14,967
Current assets		
Debtors	3,119	5,234
Short term deposits and investments (Note 4)	50,106	64,355
Cash	308	656
	53,533	70,245
Current liabilities		
Creditors: amounts falling due within one year	(8,607)	(10,544)
Net current assets	44,926	59,701
Total assets less current liabilities	57,116	74,668
Creditors: amounts falling due after more than one year	(1,683)	(2,442)
Provisions for liabilities and charges	(250)	(350)
Net assets	55,183	71,876
Capital and reserves		
Share capital	33,375	33,326
Share premium account	298,615	298,615
Other reserve	10,008	10,008
Profit and loss account	(286,815)	(270,073)
Total equity shareholders' funds	55,183	71,876

# Unaudited consolidated cash flow statement for the year ended 30 April 2002

	2002 £000	2001 £000
Net cash outflow from operating activities Returns on investments and servicing of finance Taxation – overseas Capital expenditure and financial investments	(19,309) 2,351 4 2,686	(21,738) 3,656 130 7,587
Cash utilised by operations	(14,268)	(10,365)
Management of liquid resources Financing	14,249 (342)	11,254 (381)
(Decrease)/increase in cash in the period	(361)	508
Reconciliation of net cash flow to movement in net funds (Decrease)/increase in cash in the period Cash used to decrease debt and lease financing Cash used to decrease liquid resources Exchange adjustment	(361) 462 (14,249) 18	508 402 (11,254) 62
Movement in net funds in the period Net funds at 1 May	(14,130) 62,458	(10,282) 72,740
Net funds at 30 April	48,328	62,458
Analysis of net funds Cash Short term deposits Short-term investments Bank overdraft Secured loan and finance leases	308 47,969 2,137 (16) (2,070) 48,328	656 64,355 - (21) (2,532) 62,458
		070)

#### Notes

- 1. The financial information on the Group set out above does not constitute statutory accounts within the meaning of Section 240 of the Companies Act 1985. The financial information for the year ended 30 April 2001 is extracted from the Group's audited consolidated statutory accounts. The accounts for the financial year 2002 have yet to be delivered to the Registrar of Companies and the auditor has not yet made a report for the purposes of section 249A (2) of the Companies Act 1985. The accounts for the financial year 2001 have been delivered to the Registrar and include the report of the auditors which was unqualified and did not contain a statement under Section 237 (2) or (3) of the Companies Act 1985.
- 2. The results for the year ended 30 April 2002 have been prepared in accordance with UK generally accepted accounting principles. The accounting policies applied are those set out in the Annual Report and Accounts for the year ended 30 April 2001 except that the Group has adopted Financial Reporting Standards 17: Retirement Benefits; 18: Accounting Policies; and 19: Deferred Taxation. The adoption of these standards has had no impact on the financial information set out above.
- 3. Basic and diluted losses per share are based on the loss attributable to shareholders after taxation of £16.9 million (2001: loss of £23.4 million) and on 667.2 million shares (2001: 666.4 million), being the weighted average number of shares in issue for the year.
- 4. Cash and short-term deposits have been restated for the year ended 30 April 2001. Short-term deposits are now included within short-term deposits and investments and cash consists solely of cash at bank and in hand.

# **News Release**

# **British Biotech**

23 July 2002

15

### British Biotech and BresaGen terminate E21R development agreement

British Biotech (LSE:BBG; Nasdaq:BBIOY) and BresaGen Ltd (ASX:BGN) today announced that they have terminated their collaborative agreement to develop the GM-CSF antagonist E21R.

The decision to end the collaboration follows further review of new pre-clinical study data that fail to confirm certain aspects of earlier published data on E21R-induced apoptosis in acute myeloid leukaemia (AML) cells.

As already announced with the company's preliminary financial results on 5 July 2002, British Biotech has stopped a Phase II clinical study of E21R in AML patients. In addition, the Company has now been advised by external experts that, in view of the new pre-clinical data, a proposed Phase I clinical study in children with various myeloid leukaemias could not proceed on ethical grounds. This proposed study was considered to be a pre-requisite for efficacy studies in the rare childhood disease, juvenile myelomonocytic leukaemia.

BresaGen has placed patient accrual on hold in its two clinical studies in adult chronic myelomonocytic leukaemia (CMML) and rheumatoid arthritis while it works with the Hanson Centre for Cancer Research and the Institute of Medical and Veterinary Science to review other data and discuss further the possible repetition of some of the critical pre-clinical studies.

British Biotech has written off £0.3 million in respect of the unamortised amount of milestone payments made to BresaGen. This charge, which was not included in the preliminary financial results for the year ended 30 April 2002, will be reflected in the published financial statements for the year ended 30 April 2002.

E21R was discovered by the Hanson Centre for Cancer Research of the Institute of Medical and Veterinary Science in Adelaide. The drug was licensed and developed through manufacture and Phase I testing by BresaGen and subsequently licensed to British Biotech in a collaborative development programme in which British Biotech had worldwide commercialisation rights for all clinical indications. These rights now revert to BresaGen.

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### Enquiries:

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### **Background Notes**

British Biotech's Product Portfolio now comprises four products, three in clinical development and one in late-stage pre-clinical development:

BB-10901 – A Tumour-Activated Prodrug product, currently in Phase I/II trials in small cell lung cancer. British Biotech acquired exclusive European and Japanese development and commercialisation rights to BB-10901 from ImmunoGen Inc. (Boston, USA) in May 2000.

MG98 – A 2nd generation antisense inhibitor of DNA methyltransferase, a nuclear enzyme implicated in uncontrolled tumour growth. British Biotech acquired exclusive European development and commercialisation rights to MG98 from MethylGene Inc. (Montreal, Canada) in February 2002.

BB-10153 – A novel thrombolytic, in Phase II proof-of-principle studies in heart attack patients. The study is being conducted by the Thrombolysis in Myocardial Infarction Study Group, a US-based investigative team at the forefront of clinical research into acute coronary syndromes.

BB-83698 – Targeted at community-acquired pneumonia (hospitalised patients), BB-83698 is the lead peptide deformylase inhibitor from British Biotech's Antibiotic Programme. In completed pre-clinical studies BB-83698 has shown high potency against a range of gram positive bacteria, including several drug-resistant strains. The toxicology studies necessary to allow human dosing have been carried out and final analysis of data is nearing completion. A Phase I clinical study in healthy volunteers, to determine the safety and pharmacokinetics of single doses of an intravenous formulation, is expected to begin in October 2002.

This news release contains forward-looking statements that reflect the Company's current expectations regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the success of the Company's research strategies, the applicability of the discoveries made therein, the successful and timely completion of clinical studies and the uncertainties related to the regulatory process.

# **News Release**



8 August, 2002

# British Biotech and ImmunoGen, Inc. announce initiation of second Phase I study of BB-10901

New study explores more intensive dosing regimen

British Biotech plc (LSE: BBG, Nasdaq: BBIOY) and ImmunoGen, Inc. (Nasdaq: IMGN) announced today that patient treatment has begun in the planned second Phase I study of BB-10901, a novel anti-cancer agent targeted at small cell lung cancer that uses a humanised monoclonal antibody to deliver a highly potent chemotherapeutic agent specifically to the site of the tumour.

The study is assessing daily dosing of the product and complements a weekly dosing Phase I study currently under way in the United States. It is being conducted at the Christie Hospital in Manchester, under the direction Dr Paul Lorigan and Dr Malcolm Ranson of the Department of Medical Oncology, and at Nottingham City Hospital, under the direction of leading cancer expert Professor James Carmichael and Dr Penella Woll.

The open-label, dose-escalation study will assess the safety, tolerability, and pharmacokinetics of increasing doses of BB-10901; evidence of biological activity will also be determined. The drug will be administered daily for three successive days followed by an 18-day follow-up period. As in the US Phase I study, eligible patients have relapsed or refractory small cell lung cancer, or other tumours that express the CD56 antigen targeted by the drug's antibody component. Dosage will be increased in each new cohort of patients until dose-limiting toxicity occurs and the maximum tolerated dose is established.

The study is expected to be completed by mid-2003, with results available later that year, although timing is dependent on the rate of patient recruitment and the extent of dose escalation.

Commenting on the study, Dr Elliot Goldstein, Chief Executive of British Biotech, said: "We have made good progress in the US with our trial of this novel agent. In this study we aim to find out whether a more frequent dosing regimen can be safely employed. We expect that the data from these two Phase I studies will provide the information needed to select the optimum dosing regimen to take forward into Phase II antitumour efficacy studies."

Mitchel Sayare, PhD., Chairman and Chief Executive Officer of ImmunoGen, said: "We are pleased with the progress being made by British Biotech. The data from the US Phase I study with BB-10901 are encouraging and, combined with the data this study is expected to yield, should establish the appropriate dosing schedule for future studies with the product. This study also marks the first clinical trial to be conducted with an ImmunoGen Tumour-Activated Prodrug product in Europe."

British Biotech acquired rights to develop and commercialise BB-10901 for Europe and Japan under a May 2000 agreement with ImmunoGen Inc., of Cambridge, Massachusetts. ImmunoGen retained commercialisation rights for the US and the rest of the world.

### For British Biotech plc

This news release contains forward-looking statements that reflect the Company's current expectations regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the success of the Company's research strategies, the applicability of the discoveries made therein, the successful and timely completion of clinical studies and the uncertainties related to the regulatory process.

### For ImmunoGen, Inc.

This press release includes forward-looking statements based on management's current expectations. Factors that could cause future results to differ materially from such expectations include, but are not limited to: the success of the Company's research strategy; the applicability of the discoveries made therein; the difficulties inherent in the development of pharmaceuticals, including uncertainties as to the timing and results of preclinical studies; delayed achievements of milestones; reliance on collaborators; uncertainty as to whether the Company's potential products will succeed in entering human clinical trials and uncertainty as to the results of such trials; uncertainty as to whether adequate reimbursement for these products will exist from the government, private healthcare insurers and third-party payors; the uncertainties as to the extent of future government regulation of the pharmaceutical business; and other factors described in ImmunoGen's periodic filings with the Securities and Exchange Commission.

### **Enquiries:**

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Media contacts for British Biotech

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### **Background Notes**

#### 1. BB-10901

BB-10901 is an immunoconjugate of the humanised monoclonal antibody, huN901, which binds to a particular protein found on the surface of certain tumour cells, and a powerful cytotoxic agent, DM1. Thus, it is designed to selectively seek out and kill certain types of cell, including those found in small cell lung cancer (SCLC) tumours. In pre-clinical studies, BB-10901 eradicated SCLC tumours. Under the same experimental conditions, other chemotherapies used to treat SCLC, such as cisplatin and etoposide produced only a temporary interruption of tumour growth. [Chari, R. V. J., et. al. Proceedings AACR, 2001, Abstract 4405; Liu, C., et.al. Proceedings AACR, 1997, Abstract 190]

Earlier this year, data from the ongoing U.S. Phase I study of BB-10901 were presented at the 2002 Annual Meeting of the American Society of Clinical Oncology (ASCO). The presentation included data on the product's pharmacokinetics and tolerability; initial evidence of biological activity was also presented. Patients in this study are now being dosed at 75 mg/m<sup>2</sup>.

### 2. ImmunoGen, Inc.

ImmunoGen, Inc. develops innovative biopharmaceuticals for the treatment of cancer. The Company's Tumour-Activated Prodrug (TAP) technology couples highly potent cytotoxic agents with tumour-targeting antibodies to create effective new treatments for cancer with minimal damage to normal tissue. Two TAP products developed by ImmunoGen are in clinical trials – huN901-DM1/BB-10901 and cantuzumab mertansine; the latter is licensed to GlaxoSmithKline.

#### 3. British Biotech

British Biotech is a research and development stage pharmaceuticals company aiming to develop and commercialise specialist drugs for serious illnesses, principally cancer. It currently has four products in or near to patient trials, supplemented by focused drug discovery research programmes.

### **Product Portfolio**

BB-10901 – A Tumour-Activated Prodrug product, currently in Phase I/II trials in small cell lung cancer. British Biotech acquired exclusive European and Japanese development and commercialisation rights to BB-10901 from ImmunoGen Inc. (Boston, USA) in May 2000.

MG98 – A 2nd generation antisense inhibitor of DNA methyltransferase (DNMT), a nuclear enzyme implicated in uncontrolled tumour growth. British Biotech acquired exclusive European development and commercialisation rights to MG98 from MethylGene Inc. (Montreal, Canada) in February 2002.

BB-10153 – A novel thrombolytic, about to start a Phase II proof-of-principle study in heart attack patients. The study will be conducted by the Thrombolysis in Myocardial Infarction Study Group, a US-based investigative team at the forefront of clinical research into acute coronary syndromes.

BB-83698 –A peptide deformylase inhibitor targeted at community-acquired pneumonia (hospitalised patients). In completed pre-clinical studies BB-83698 has shown high potency against a range of gram positive bacteria, including several drug-resistant strains. A Phase I clinical study in healthy volunteers, to determine the safety and pharmacokinetics of single doses of an intravenous formulation, is expected to begin in October 2002.

#### Research

Antibiotic Programme – A research programme into the use of inhibitors of peptide deformylase and other bacterial metalloenzymes to treat infectious disease. The programme has produced several lead compounds in research and pre-clinical development, with high potency shown against drug resistant gram-positive and gram-negative pathogens.

Anti-Inflammatory Programme – Working in collaboration with Serono SA, this research programme is investigating the use of metalloenzyme inhibitors as new treatments for serious inflammatory diseases, particularly multiple sclerosis.

Cancer Programme – As part of its collaboration with MethylGene on MG98 (see above) British Biotech has an exclusive option to European development and commercialisation rights for compounds from MethylGene's research into small molecule inhibitors of DNMT.

Biodefence Research – As part of the UK Government's biodefence initiative, the Defence, Science and Technology Laboratory (DSTL) of Porton Down is investigating the utility of selected British Biotech metalloenzyme inhibitors against anthrax lethal toxin and botulin toxin.

# **News Release**

# **British Biotech**

For release: 9 August 2002

# British Biotech and GeneSoft collaborate to discover and develop novel antibiotics

### First in class product expected in clinic by Q4 2002

British Biotech plc (LSE: BBG, Nasdaq: BBIOY) and GeneSoft Inc. announced today that they have signed agreements for a broad-based collaboration to discover and develop novel anti-infective drugs based on British Biotech's proprietary bacterial metalloenzyme inhibitors.

Combining British Biotech's novel targets, chemistry and clinical development with GeneSoft's experience in antibiotic lead optimisation and clinical expertise, the collaboration will focus on three specific areas:

- clinical development and marketing of BB-83698, British Biotech's lead peptide deformylase (PDF) inhibitor, governed by a licence, development and commercialisation agreement;
- lead optimisation and clinical development of oral PDF inhibitors, governed by a research agreement; and
- drug discovery research exploiting British Biotech's portfolio of intellectual property and expertise in respect of other microbial metalloenzyme targets, governed by a research agreement.

GeneSoft will make an initial payment to British Biotech of US\$4 million. On commencement of a Phase I study of BB-83698, anticipated in October 2002, GeneSoft will pay British Biotech a further US\$1 million and equity representing 3.45 per cent of GeneSoft.

"GeneSoft is delighted to partner with British Biotech to discover and develop new antibiotics," said Gary Patou, MD, GeneSoft's President. "The medical community desperately needs new mechanism of action antibiotics to combat multidrug resistant bacteria. We believe that the programmes developed within British Biotech have tremendous potential to bring new antibiotics to patients."

Welcoming the agreement, British Biotech Chief Executive Dr Elliot Goldstein said: "Through this collaboration British Biotech has achieved its three key objectives of expanding the Antibiotic Programme, while sharing the costs and commercialisation rights. GeneSoft is an ideal partner for the programme. It specialises in antibiotic drug discovery and development and brings a wealth of clinical and scientific expertise in this field."

#### BB-83698

BB-83698 represents a new class of antibiotic and is targeted at hospitalised patients with community-acquired pneumonia. A Phase I clinical study in healthy volunteers, to determine safety and pharmacokinetics of single doses of an intravenous formulation, is expected to begin in October 2002.

Under the first part of the collaboration, British Biotech and GeneSoft have entered into an exclusive agreement to co-develop and commercialise BB-83698. The development costs will be shared equally by British Biotech and GeneSoft, as will the world-wide profits.

### PDF research programme

In support of BB-83698, British Biotech and GeneSoft have entered into an exclusive research agreement, for an initial period of three years, to identify further PDF inhibitors for clinical development, including oral inhibitors for broader indications. The collaboration will allow increased resource and capabilities to be applied to the PDF programme to exploit fully the potential of this novel series of agents. British Biotech will maintain resources on this programme at current levels with GeneSoft adding resource equivalent to 170 per cent of British Biotech's. As with BB-83698, development costs and world-wide profits are shared equally.

### Other metalloenzyme targets

GeneSoft will select from British Biotech's other anti-microbial metalloenzyme programmes, and determine the research projects that it wishes to progress. British Biotech will receive undisclosed milestone and royalty payments on the successful development and commercialisation of any products from each research project.

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### Enquiries:

British Biotech plc

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Joanne DelRosario

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This news release contains forward-looking statements that reflect the Company's current expectations regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the success of the Company's research strategies, the applicability of the discoveries made therein, the successful and timely completion of clinical studies and the uncertainties related to the regulatory process.

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### **Background Notes**

### 1. The need for new antibiotics

One of the key contributors to morbidity and mortality due to bacterial infections is the increasing prevalence of drug-resistant bacteria. The combination of a limited number of targets, widespread use of prophylactic therapy, empirical treatment with broad-spectrum agents, and the natural evolution of bacteria, has contributed to a resurgence of antibiotic resistance and the creation of a major public health problem. New structural classes of antibiotics that target alternative, essential bacterial processes are likely to make significant inroads into the anti-infectives market.

Bacterial genomes contain a number of metalloenzymes, several of which are believed to be essential to survival, and bacterial polypeptide deformylase (PDF) is now widely recognised as an attractive target for antibacterial chemotherapy (Giglione *et al*, 2001 *Molecular Microbiology*, vol 36, 1197-205). Deformylation is a crucial step in bacterial protein biosynthesis and the PDF enzyme is essential for bacterial growth, with the gene encoding PDF (def) found to be present in all sequenced path'ogenic bacterial genomes.

In research and pre-clinical studies, British Biotech's PDF inhibitors have shown a microbiological activity profile suitable for respiratory tract pathogens and high potency against antibiotic-resistant organisms. BB-83698, the company's lead PDF inhibitor compound, has now completed the toxicology studies necessary to allow human dosing and a Phase I clinical study in healthy volunteers, to determine the safety and pharmacokinetics of single doses of an intravenous formulation, is expected to begin in October 2002.

### 2. GeneSoft Inc

GeneSoft is a privately held biopharmaceutical company headquartered in South San Francisco, California. GeneSoft was founded in 1998 by Peter Dervan, Ph.D. and others based on proprietary chemistry technology licensed from the California Institute of Technology. GeneSoft has been using its proprietary technology to discover and develop novel anti-infective products, and currently has a portfolio of lead compounds in late pre-clinical studies. Since its founding, GeneSoft has raised over \$60 million in equity capital from investors in the United States, Europe and Asia.

For more information please visit www.genesoft.com

### 3. British Biotech

British Biotech is a research and development stage pharmaceuticals company aiming to develop and commercialise specialist drugs for serious illnesses, principally cancer. It currently has four products in or near to patient trials, supplemented by focused, collaborative drug discovery research programmes.

#### **Product Portfolio**

BB-10901 – A Tumour-Activated Prodrug product, currently in Phase I/II trials in small cell lung cancer. British Biotech acquired exclusive European and Japanese development and commercialisation rights to BB-10901 from ImmunoGen Inc. (Boston, USA) in May 2000.

MG98 – A 2nd generation antisense inhibitor of DNA methyltransferase (DNMT), a nuclear enzyme implicated in uncontrolled tumour growth. British Biotech acquired exclusive European development and commercialisation rights to MG98 from MethylGene Inc. (Montreal, Canada) in February 2002.

BB-10153 – A novel thrombolytic, about to start a Phase II proof-of-principle study in heart attack patients. The study will be conducted by the Thrombolysis in Myocardial Infarction Study Group, a US-based investigative team at the forefront of clinical research into acute coronary syndromes.

BB-83698 –A peptide deformylase inhibitor targeted at community-acquired pneumonia (hospitalised patients). (See above.)

### Research

Antibiotic Programme – Now working in collaboration with Genesoft, this research programme is focused on the development of bacterial metalloenzyme inhibitors as novel anti-infective drugs (see above).

Anti-Inflammatory Programme – In collaboration with Serono SA, this research programme is investigating the use of metalloenzyme inhibitors as new treatments for serious inflammatory diseases, particularly multiple sclerosis.

Cancer Programme – As part of the collaboration with MethylGene on MG98 (see above) British Biotech has an exclusive option to European development and commercialisation rights for compounds from MethylGene's research into small molecule inhibitors of DNMT.

Biodefence Research – As part of the UK Government's biodefence initiative, the Defence, Science and Technology Laboratory (DSTL) of Porton Down is investigating the utility of selected British Biotech metalloenzyme inhibitors against anthrax lethal toxin and botulin toxin.

# **British Biotech**

3<sup>rd</sup> July 2002

Company Announcements Office Stock Exchange London EC2N 1HP

Dear Sir,

Pursuant to the terms of remuneration agreed between British Biotech plc and its subsidiaries ("British Biotech") and its Chairman, Mr Chris Hampson, it is announced that Mr Hampson, on 3<sup>rd</sup> July 2002, acquired 39,533 ordinary shares in British Biotech at a price of 7.5p per share.

Following this purchase, Mr Hampson is interested in a total of 683,491 ordinary shares.

Yours faithfully

Legal Counsel

# **British Biotech**

12<sup>th</sup> August 2002

Securities and Exchange Commission 450 Fifth Street, N.W. Washington, DC 20549 U.S.A.



### Dear Sirs

On behalf of British Biotech plc, I furnish herewith eight copies of Form 6-K for the period 1<sup>st</sup> July 2002 to 31<sup>st</sup> July 2002 one of which is manually signed (and sequentially numbered) and seven of which are conformed.

Please have the attached copy of this letter stamped to indicate its receipt and returned to me at the address shown below.

Please telephone me at 011 44 865 748 747 with any questions or comments you may have regarding this form.

Yours faithfully

Tony Weir

Finance Director

cc: NASD (3 copies)

### FORM 6-K

SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

Pursuant to Rule 13a-16 or 15d-16 of the Securities Exchange Act of 1934

Report of Foreign Issuer for the period of 1st July 2002 to 31st July 2002



### British Biotech plc

Thames Court Watlington Road Oxford OX4 6LY England

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20F or Form 40F.

Form 20F	X	Form 40F
<del>-</del>		

Indicate by check mark whether the registrant by furnishing the information contained in this Form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes	No	X

If "Yes" is marked, indicate below the file number assigned to the registrant in connection with Rule 12g3-2(b): 82 - \_\_\_\_

### **SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

### **BRITISH BIOTECH PLC**

(Registrant)

By: 1. 1. Let Date: 12th August 2002

Name: Tony Weir

Title: Finance Director

# **News Release**

# **British Biotech**

5 July 2002

# British Biotech plc: Preliminary financial results for the year ended 30 April 2002

British Biotech plc (LSE: BBG, Nasdaq: BBIOY) today announced its preliminary financial results for the year ended 30 April 2002.

### **Business highlights**

- BB-10901
  - Phase I/II study under way in relapsed/refractory small cell lung cancer (weekly dosing)
  - CTX granted for UK Phase I study
- E21R
  - Phase II study stopped in acute myeloid leukaemia
  - Phase II study continuing in chronic myelomonocytic leukaemia
  - Orphan drug designation for juvenile myelomonocytic leukaemia (EU)
- BB-10153
  - Successful manufacturing campaign
  - Phase II proof-of-principle study in acute myocardial infarction to start July 2002
- Product Portfolio expanded with the grant of European development and commercialisation rights to MG98 from MethylGene Inc.
- Antibiotic Programme
  - BB-83698 to start Phase I by October 2002
  - Nine presentations at 41<sup>st</sup> ICAAC (December 2001); eight presentations accepted for 42<sup>nd</sup> ICAAC (September 2002)
- Biodefence research agreement with UK Government's Defence Science and Technology Laboratory
- Batimastat BiodivYsio® stent
  - Development suspended
- Final stage of restructuring completed with the sale of non-core assets to OSI
   Pharmaceuticals, Inc., and the successful recruitment of experienced pharmaceutical industry executives into key operational roles

## Financial highlights

- Loss for the year reduced to £16.9 million (2001: £23.4 million)
- Annual cash burn of £14.6 million (2001: £10.7 million)
- Cash and short term investments of £50.4 million at 30 April 2002

Commenting on the year's results, Dr Elliot Goldstein, Chief Executive Officer of British Biotech, said: "In a challenging economic environment for biotechnology companies, British Biotech continues to make progress. With products in the clinic, strong development capabilities and cash, British Biotech is well placed for strategic initiatives in Europe and North America that will strengthen our platform for growth and the creation of shareholder value."

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### For further information, please contact:

In the UK:

British Biotech plc

Tel: 01865 748747 Dr Elliot Goldstein, Chief Executive Officer Tony Weir, Finance Director

### Hogarth Partnership

Tel: 020 7357 9477 John Olsen, Georgina Briscoe

In the USA: GA Kraut

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Duke Coffey

This news release contains forward-looking statements that reflect the Company's current expectation regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the success of the Company's research strategy, the applicability of the discoveries made therein, the successful and timely completion of clinical studies and the uncertainties related to the regulatory process.

### British Biotech plc ("British Biotech")

### Preliminary results for the year ended 30 April 2002

### 1. Business Review

### Company Strategy

British Biotech's strategy is to create long-term value for shareholders by building a product portfolio of innovative medicines, targeted mainly at cancer but based on a variety of technologies, and to bring these to market as expeditiously as possible. The Company has retained commercialisation rights, in various territories, to all of the products in the portfolio and value will be created as the Company generates data from later-stage clinical trials over the next three years.

The Company adopts a highly rigorous approach to its development activities. Should any product fail to meet its clinical endpoints, development will cease and it will be dropped from the portfolio. The portfolio will continue to be expanded by drug development candidates emerging from in-house research and by the acquisition of rights to products discovered by other companies. The Company is actively seeking further collaborations where it can apply its development capabilities to create additional value. Additionally, the Board is looking at ways in which the Company can enhance shareholder value by combining its own portfolio, development capabilities and cash with those of other businesses in Europe and North America.

### Restructuring

In August 2001 British Biotech completed the final stage in its restructuring programme, enabling it to intensify its focus on drug development, add to cash resources, and reduce significantly its fixed infrastructure costs.

Under an agreement with OSI Pharmaceuticals, Inc., (Nasdaq: OSIP), British Biotech transferred part of its pre-clinical research facilities to OSI, including 59 employees, leases on two properties, and fixed assets with a net book value of £5.0 million. British Biotech received £8.7 million in cash and reduced the Company's fixed infrastructure costs by £6.0 million per annum. Following the restructuring, British Biotech had 87 full-time employees at 30 April 2002.

### People

In line with its focus on products, British Biotech has sought to strengthen its development capabilities, and has been successful in recruiting experienced executives from established pharmaceutical companies such as Pfizer, Glaxo SmithKline, Novartis and Johnson & Johnson to key managerial and operational roles in clinical development, business development and regulatory affairs. The Company has also expanded its chemistry and pharmaceutical development functions to support its research and development of novel antibiotics and for its collaborative research with Serono into anti-inflammatory treatments.

### **Product Portfolio**

British Biotech's Product Portfolio currently comprises four drugs in clinical development and one product in late-stage pre-clinical development.

Product/ Partner	Indications	Clinical Development Status	Commercial Rights	Next Milestones
BB-10901 ImmunoGen Inc. (USA)	Small cell lung cancer Neuroendocrine tumours Carcinoid	Currently in Phase I to establish maximum tolerated dose (weekly dosing)  CTX granted for UK Phase I study (more frequent dosing)	■ Europe, Japan	Start Phase I (UK) Q3 2002 Start Phase II Q4 2002
E21R BresaGen Ltd (Australia)	■ CMML ■ JMML (EU orphan status designation)	<ul> <li>AML Phase II study stopped</li> <li>CMML pilot Phase II study ongoing</li> <li>JMML development under discussion with regulators and external experts</li> </ul>	•Global	Start JMML development Q3 2002 CMML Phase II results Q4 2003
MG98 MethylGene Inc. (Canada)	Gastric cancer AML/MDS Other cancers involving hyper- methylation	<ul> <li>AML/MDS Phase I dose and schedule optimising study study ongoing</li> <li>Head/neck cancer, renal carcinoma Phase II studies – recruitment closed</li> </ul>	■ Europe	Start European studies Q4 2002
BB-10153	<ul> <li>Acute myocardial infarction</li> <li>Stroke</li> <li>Peripheral arterial occlusion</li> </ul>	Phase II in AMI to start in July (in collaboration with TIMI Study Group)	■ Global	Phase II data Q2 2003
BB-83698	Community-acquired pneumonia (hospitalised patients)	■Pre-clinical	■Global	Start Phase I i.v. study October 2002

**BB-10901** – BB-10901 is being developed jointly by British Biotech and the US biotechnology company ImmunoGen, Inc (Nasdaq: IMGN). It is an immunoconjugate of the cytotoxic maytansinoid drug, DM1, with the humanized monoclonal antibody huN901 and is designed to selectively kill certain types of cancer cells including those found in small cell lung cancer (SCLC). In pre-clinical studies, and in contrast to current cytotoxic therapy, BB-10901 completely eradicated SCLC tumours.

In May 2001, British Biotech began a combined Phase I/II clinical study at two centres in the USA to evaluate the safety, tolerability and biological activity of weekly infusions of BB-10901. Initial Phase I data were presented at the 2002 meeting of the American Society of Clinical Oncology. These showed the drug was well tolerated, with no dose-limiting toxicity, at weekly doses up to and including  $60 \text{mg/m}^2$ . Recruitment of patients at the sixth dose level of  $75 \text{mg/m}^2$  is continuing. Once the maximum tolerated dose has been established, an additional 29 patients will be treated at that dose in the Phase II portion of the study. This progression to Phase II is

In April 2002, the UK's Medicines Control Agency granted a Clinical Trials Exemption (CTX) to British Biotech for a Phase I study of BB-10901 to investigate the safety of the drug when administered on a more frequent dosing regime. This study is expected to start shortly; further details will be published when the study begins.

British Biotech has commercialisation rights for BB-10901 in Europe and Japan. ImmunoGen retained rights for America and the rest of the world.

**E21R** – E21R is a modified form of granulocyte-macrophage colony-stimulating factor (GM-CSF) being developed in collaboration with the Australian biotechnology company, BresaGen Ltd. (ASX: BGN).

BresaGen completed Phase I clinical testing of E21R in 2000. In August 2001, British Biotech started a Phase II study to investigate E21R's efficacy, safety, tolerability and pharmacokinetics in patients with acute myeloid leukaemia (AML). This study has now been stopped since new pre-clinical data have failed to support the previous high incidence of apoptosis (cell killing) in AML. Further pre-clinical studies are under way to assess the rationale for development of E21R in AML.

These new pre-clinical data do not call into question the rationale for development of E21R in chronic myelomonocytic leukaemia (CMML) and juvenile myelomonocytic leukaemia (JMML). BresaGen is continuing to recruit patients to a pilot Phase II study in CMML. Also, in March 2002, the European Commission designated E21R as having orphan drug status for the treatment of JMML, a rare and deadly disease affecting very young children. The orphan designation is based on the rare and serious nature of the disease, the lack of satisfactory therapy and the product's potential to have significant therapeutic benefit. Discussions with regulators and clinical experts on the appropriate clinical development programme in JMML are ongoing.

Under its collaboration with BresaGen, British Biotech has exclusive world-wide rights to commercialise E21R for all indications.

MG98 – In February 2002, British Biotech was granted European development and commercialisation rights for MG98, a novel second-generation antisense compound discovered by MethylGene Inc., a privately-held Canadian company. MG98 is designed to inhibit the expression of DNA methyltransferase (DNMT), an enzyme implicated in uncontrolled tumour growth. MethylGene granted North American development and commercialisation rights for MG98 to MGI PHARMA in August 2000.

During the Phase I trials of MG98, one patient receiving MG98 under a twice-weekly regimen experienced a sustained (>6 months) objective partial response (>70% reduction in the sum of bidimensional products of measurable lesions). This regimen was well tolerated in the all-comer solid tumour population examined, and this regimen was chosen for use in the first Phase II trials.

Two such North American Phase II studies investigating twice-weekly administration of MG98 monotherapy in patients with head and neck cancer (conducted by MethylGene) and renal cell carcinoma (sponsored by MethylGene in collaboration with the National Cancer Institute of Canada Clinical Trials Group) have closed recruitment. In these studies MG98, at the doses and twice-weekly schedule tested, did not demonstrate objective clinical responses as defined by the

A Phase I trial investigating multiple doses and schedules in patients with advanced myelodysplasia and acute myeloid leukaemia, in order to optimise dose and schedule for additional trials, was initiated by MGI PHARMA in January 2002 and continues to recruit patients. British Biotech plans to initiate in Q4 2002 a further Phase I study to investigate the safety and tolerability of a continuous infusion regimen in patients with solid tumours such as gastric adenocarcinoma. Results from these Phase I studies will form the basis of any future Phase II programme.

**BB-10153** – BB-10153 is a novel thrombolytic (clot-busting) agent discovered by British Biotech. It is an engineered form of human plasminogen, modified so that it is activated to plasmin by thrombin, which is only produced at the site of fresh blood clots, rather than by the body's natural plasminogen activators such as tPA. Pre-clinical testing showed that BB-10153 only dissolves recently-formed or still-forming clots. A Phase I study, at doses up to 4.8mg/kg, demonstrated the drug to be safe in healthy volunteers.

During the year in review, GMP production of material for a Phase II study was completed and in March 2002, the US Food & Drug Administration gave the go-ahead to test BB-10153 in heart attack patients. Supplies of the drug and the necessary approvals are now in place to begin this study, which will be conducted by the US-based Thrombolysis in Myocardial Infarction (TIMI) Study Group. The study will test the ability of BB-10153, given at doses between 1 and 5mg/kg, to dissolve clots and restore blood flow in the coronary arteries of heart attack patients. The study will also evaluate the safety of treatment with BB-10153, especially with respect to bleeding.

Data from the study are expected to be available in mid-2003 and will be used to attract potential collaborators for continued development and commercialisation of this product.

BB-83698 – Targeted at community-acquired pneumonia (hospitalised patients), BB-83698 is the lead peptide deformylase inhibitor from British Biotech's Antibiotic Programme. In completed pre-clinical studies BB-83698 has shown high potency against a range of gram positive bacteria, including several drug-resistant strains. The toxicology studies necessary to allow human dosing have been carried out and final analysis of data is nearing completion. A Phase I clinical study in healthy volunteers, to determine the safety and pharmacokinetics of single doses of an intravenous formulation, is expected to begin in October 2002.

### Other Product Development Programmes

Batimastat Biodiv Ysio® stent — Clinical development of this product was suspended in March 2002 pending further review of data from the BRILLIANT I clinical trial. BRILLIANT I is a 150 patient multi-centre open clinical trial, recruitment for which was completed in November 2001. Six-month angiographic and clinical follow-up on an initial group of patients from this trial indicated that the product was unlikely to show the benefit that was evident in the pre-clinical studies. Additional patient data is being collected and analysed, after which a final decision will be made to continue or end this programme.

#### Research

Antibiotic Programme – British Biotech's research into antibiotics is founded on the Company's strong intellectual property position in bacterial metalloenzyme inhibitors. The programme has produced several lead compounds in research and pre-clinical development, with

In December 2001 Company researchers and external scientific collaborators presented details of this research at the 41<sup>st</sup> Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). The presentations covered the *in vitro* and *in vivo* efficacy of British Biotech's peptide deformylase inhibitor compounds against a variety of drug-resistant pathogens; research into the antibiotic activity and characterisation of inhibitors of the 'LpxC' metalloenzyme; and the use of bio-informatics in the Company's antibiotic drug discovery programme.

British Biotech will be giving a further update on its Antibiotic Programme at the 42<sup>nd</sup> ICAAC (San Diego, 27-30 September 2002), where eight presentations have been accepted.

Serono Collaboration – The research collaboration formed in October 2000 between British Biotech and Serono SA (SWX: SEO, NYSE: SRA) to identify new treatments for serious inflammatory diseases, particularly multiple sclerosis, has made good progress. The two companies have completed screening of British Biotech's compound library against pathologically relevant metalloenzyme targets, and identified selective inhibitors active against three enzyme targets involved in inflammatory indications.

Cancer Programme – In February 2002, British Biotech was granted an exclusive one year option, renewable for a second year, for European development and commercialisation rights of compounds from MethylGene's research programme into small molecule inhibitors of DNA methyltransferase.

**Biodefence Research Initiative** – As part of the UK Government's biodefence initiative, the Company has entered into an agreement with the Defence, Science and Technology Laboratory (DSTL) of Porton Down to investigate the utility of selected British Biotech metalloenzyme inhibitors against anthrax lethal toxin and botulin toxin.

#### Other matters

The Company has noted the recent press comment regarding Class Law, an English firm of solicitors, and putative claims against the Company in respect of events more than four years ago. The Company understands that Class Law has been attempting to solicit interest in such claims since at least February 2001 and since such time has also been regularly suggesting that proceedings against the Company are imminent. Such proceedings have not been forthcoming. The Company has considered the nature of Class Law's putative, but unspecified, claims with its legal advisers and believes them to be without merit or foundation.

## 2. Objectives

The principal objectives for the current financial year are:

- Meet the product development milestones detailed in the table above;
- Add at least one new product to the portfolio through collaboration;
- Form a collaboration on the Antibiotic Programme;
- Explore strategic growth opportunities, in particular mergers or acquisitions.

### 3. Financial review

#### Profit and loss account

The loss for the year ended 30 April 2002 decreased to £16.9 million (2001: £23.4 million) due to reduced levels of expenditure and the profit arising from the restructuring and the transfer, in August 2001, of certain pre-clinical facilities to OSI Pharmaceuticals, Inc. Research and development tax credits of £1.6 million were recognised in the year (2001: £nil), as the Company believes it has satisfied the requirements of the Finance Act 2000 for the year ended 30 April 2002.

Turnover in the year amounted to £1.5 million (2001: £1.6 million). The turnover resulted principally from the agreement with Serono to research, develop and commercialise metalloenzyme inhibitors in serious inflammatory disease, with £1.4 million (2001: £1.3 million) of the £3.3 million received from Serono in November 2000 recognised as income in the year. Research and development expenditure for the year was £2.7 million lower at £21.0 million (2001: £23.7 million) due to lower infrastructure costs following the restructuring in August 2001.

Administrative expenses for the year were lower at £3.8 million (2001: £4.0million) including a charge of £0.2 million (2001: £nil) in respect of share options. The lower expenditure is due to savings from the restructuring implemented in August 2001. Profit of £2.5 million on the disposal of fixed assets arose on the restructuring from the transfer of certain pre-clinical facilities to OSI. The amortisation of intangible fixed assets was £0.2 million (2002: £0.1 million).

Interest receivable was £2.8 million (2001: £3.8 million) with the reduction due to lower interest rates and lower average cash balances during the year. Amounts written off investments in the year were £ 0.3 million (2001: £0.8 million).

#### Cash flow

The reduction in cash and short term investment balances during the year was £14.6 million (2001: £10.7 million) comprising cash utilised by operations of £14.3 million (2001: £10.3 million) and financing repayments of £0.3 million (2001: £0.4 million). The cash utilised by operations benefited from the receipt of £8.7 million from OSI in 2002 and from the proceeds of the sale and leaseback of the office facility of £11.2 million in 2001. Excluding these amounts, the cash utilised by operations was £23.0 million (2001: £21.5 million). The increase was due to lower interest received of £1.3 million, increased capital expenditure of £0.8 million on the fitout of laboratories and offices following the OSI transaction and additional expenditure on the Product Portfolio of £2.6 million. These were offset by lower infrastructure costs in the second half of the year of £3.0 million following the restructuring. These lower infrastructure costs represent a permanent annualised cost saving of some £6 million.

Cash and short-term investments at 30 April 2002 were £50.4 million, compared with £65 million at 30 April 2001.

# Unaudited consolidated profit and loss account for the year ended 30 April 2002

	2002 £000	2001 £000
Turnover	1,450	1,588
Research and development expenditure Administrative expenses	(20,955) (3,759)	(23,724) (3,997)
Operating loss	(23,264)	(26,133)
Profit on disposal of fixed assets Interest receivable Amount written off investments Interest payable	2,505 2,820 (324) (278)	3,778 (799) (329)
Loss on ordinary activities before taxation	(18,541)	(23,483)
Taxation	1,608	130
Loss for the financial year transferred to reserves	(16,933)	(23,353)
Loss per share (basic and diluted) (Note 3)	(2.5)p	(3.5)p

# Unaudited statement of total recognised gains and losses for the year ended 30 April 2002

	2002 £000	2001 £000
Consolidated loss for the financial year Translation of overseas subsidiary financial statements	(16,933)	(23,353) 25
Total recognised losses relating to the year	(16,930)	(23,328)

# Unaudited consolidated balance sheet as at 30 April 2002

	2002	2001 Restated
	£002	(Note 4)
	2000	£000
Fixed assets		
Intangible assets	2,288	1,090
Tangible assets	7,996	13,053
Investments	1,906	824
•	12,190	14,967
Current assets		
Debtors	3,119	5,234
Short term deposits and investments (Note 4)	50,106	64,355
Cash	308	656
	53,533	70,245
Current liabilities		
Creditors: amounts falling due within one year	(8,607)	(10,544)
Net current assets	44,926	59,701
Total assets less current liabilities	57,116	74,668
Creditors: amounts falling due after more than one year	(1,683)	(2,442)
Provisions for liabilities and charges	(250)	(350)
Net assets	55,183	71,876
Capital and reserves		
Share capital	33,375	33,326
Share premium account	298,615	298,615
Other reserve	10,008	10,008
Profit and loss account	(286,815)	(270,073)
Total equity shareholders' funds	55,183	71,876

# Unaudited consolidated cash flow statement for the year ended 30 April 2002

	2002 £000	2001 £000
Net cash outflow from operating activities Returns on investments and servicing of finance Taxation – overseas Capital expenditure and financial investments	(19,309) 2,351 4 2,686	(21,738) 3,656 130 7,587
Cash utilised by operations	(14,268)	(10,365)
Management of liquid resources Financing	14,249 (342)	11,254 (381)
(Decrease)/increase in cash in the period	(361)	508
Reconciliation of net cash flow to movement in net funds (Decrease)/increase in cash in the period Cash used to decrease debt and lease financing Cash used to decrease liquid resources Exchange adjustment	(361) 462 (14,249) 18	508 402 (11,254) 62
Movement in net funds in the period Net funds at 1 May	(14,130) 62,458	(10,282) 72,740
Net funds at 30 April	48,328	62,458
Analysis of net funds Cash Short term deposits Short-term investments Bank overdraft Secured loan and finance leases	308 47,969 2,137 (16) (2,070) 48,328	656 64,355 - (21) (2,532) 62,458

#### Notes

- 1. The financial information on the Group set out above does not constitute statutory accounts within the meaning of Section 240 of the Companies Act 1985. The financial information for the year ended 30 April 2001 is extracted from the Group's audited consolidated statutory accounts. The accounts for the financial year 2002 have yet to be delivered to the Registrar of Companies and the auditor has not yet made a report for the purposes of section 249A (2) of the Companies Act 1985. The accounts for the financial year 2001 have been delivered to the Registrar and include the report of the auditors which was unqualified and did not contain a statement under Section 237 (2) or (3) of the Companies Act 1985.
- 2. The results for the year ended 30 April 2002 have been prepared in accordance with UK generally accepted accounting principles. The accounting policies applied are those set out in the Annual Report and Accounts for the year ended 30 April 2001 except that the Group has adopted Financial Reporting Standards 17: Retirement Benefits; 18: Accounting Policies; and 19: Deferred Taxation. The adoption of these standards has had no impact on the financial information set out above.
- 3. Basic and diluted losses per share are based on the loss attributable to shareholders after taxation of £16.9 million (2001: loss of £23.4 million) and on 667.2 million shares (2001: 666.4 million), being the weighted average number of shares in issue for the year.
- 4. Cash and short-term deposits have been restated for the year ended 30 April 2001. Short-term deposits are now included within short-term deposits and investments and cash consists solely of cash at bank and in hand.

## **News Release**

## **British Biotech**

23 July 2002

#### British Biotech and BresaGen terminate E21R development agreement

British Biotech (LSE:BBG; Nasdaq:BBIOY) and BresaGen Ltd (ASX:BGN) today announced that they have terminated their collaborative agreement to develop the GM-CSF antagonist E21R.

The decision to end the collaboration follows further review of new pre-clinical study data that fail to confirm certain aspects of earlier published data on E21R-induced apoptosis in acute myeloid leukaemia (AML) cells.

As already announced with the company's preliminary financial results on 5 July 2002, British Biotech has stopped a Phase II clinical study of E21R in AML patients. In addition, the Company has now been advised by external experts that, in view of the new pre-clinical data, a proposed Phase I clinical study in children with various myeloid leukaemias could not proceed on ethical grounds. This proposed study was considered to be a pre-requisite for efficacy studies in the rare childhood disease, juvenile myelomonocytic leukaemia.

BresaGen has placed patient accrual on hold in its two clinical studies in adult chronic myelomonocytic leukaemia (CMML) and rheumatoid arthritis while it works with the Hanson Centre for Cancer Research and the Institute of Medical and Veterinary Science to review other data and discuss further the possible repetition of some of the critical pre-clinical studies.

British Biotech has written off £0.3 million in respect of the unamortised amount of milestone payments made to BresaGen. This charge, which was not included in the preliminary financial results for the year ended 30 April 2002, will be reflected in the published financial statements for the year ended 30 April 2002.

E21R was discovered by the Hanson Centre for Cancer Research of the Institute of Medical and Veterinary Science in Adelaide. The drug was licensed and developed through manufacture and Phase I testing by BresaGen and subsequently licensed to British Biotech in a collaborative development programme in which British Biotech had worldwide commercialisation rights for all clinical indications. These rights now revert to BresaGen.

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#### Enquiries:

#### British Biotech plc

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Partnership

#### BresaGen Ltd

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## **News Release**

### **British Biotech**

8 August, 2002

# British Biotech and ImmunoGen, Inc. announce initiation of second Phase I study of BB-10901

New study explores more intensive dosing regimen

British Biotech plc (LSE: BBG, Nasdaq: BBIOY) and ImmunoGen, Inc. (Nasdaq: IMGN) announced today that patient treatment has begun in the planned second Phase I study of BB-10901, a novel anti-cancer agent targeted at small cell lung cancer that uses a humanised monoclonal antibody to deliver a highly potent chemotherapeutic agent specifically to the site of the tumour.

The study is assessing daily dosing of the product and complements a weekly dosing Phase I study currently under way in the United States. It is being conducted at the Christie Hospital in Manchester, under the direction Dr Paul Lorigan and Dr Malcolm Ranson of the Department of Medical Oncology, and at Nottingham City Hospital, under the direction of leading cancer expert Professor James Carmichael and Dr Penella Woll.

The open-label, dose-escalation study will assess the safety, tolerability, and pharmacokinetics of increasing doses of BB-10901; evidence of biological activity will also be determined. The drug will be administered daily for three successive days followed by an 18-day follow-up period. As in the US Phase I study, eligible patients have relapsed or refractory small cell lung cancer, or other tumours that express the CD56 antigen targeted by the drug's antibody component. Dosage will be increased in each new cohort of patients until dose-limiting toxicity occurs and the maximum tolerated dose is established.

The study is expected to be completed by mid-2003, with results available later that year, although timing is dependent on the rate of patient recruitment and the extent of dose escalation.

Commenting on the study, Dr Elliot Goldstein, Chief Executive of British Biotech, said: "We have made good progress in the US with our trial of this novel agent. In this study we aim to find out whether a more frequent dosing regimen can be safely employed. We expect that the data from these two Phase I studies will provide the information needed to select the optimum dosing regimen to take forward into Phase II antitumour efficacy studies."

Mitchel Sayare, PhD., Chairman and Chief Executive Officer of ImmunoGen, said: "We are pleased with the progress being made by British Biotech. The data from the US Phase I study with BB-10901 are encouraging and, combined with the data this study is expected to yield, should establish the appropriate dosing schedule for future studies with the product. This study also marks the first clinical trial to be conducted with an ImmunoGen Tumour-Activated Prodrug product in Europe."

British Biotech acquired rights to develop and commercialise BB-10901 for Europe and Japan under a May 2000 agreement with ImmunoGen Inc., of Cambridge, Massachusetts. ImmunoGen retained commercialisation rights for the US and the rest of the world.

#### For British Biotech plc

This news release contains forward-looking statements that reflect the Company's current expectations regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the success of the Company's research strategies, the applicability of the discoveries made therein, the successful and timely completion of clinical studies and the uncertainties related to the regulatory process.

#### For ImmunoGen, Inc.

This press release includes forward-looking statements based on management's current expectations. Factors that could cause future results to differ materially from such expectations include, but are not limited to: the success of the Company's research strategy; the applicability of the discoveries made therein; the difficulties inherent in the development of pharmaceuticals, including uncertainties as to the timing and results of preclinical studies; delayed achievements of milestones; reliance on collaborators; uncertainty as to whether the Company's potential products will succeed in entering human clinical trials and uncertainty as to the results of such trials; uncertainty as to whether adequate reimbursement for these products will exist from the government, private healthcare insurers and third-party payors; the uncertainties as to the extent of future government regulation of the pharmaceutical business; and other factors described in ImmunoGen's periodic filings with the Securities and Exchange Commission.

#### **Enquiries:**

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#### ImmunoGen Inc.

Carol Hausner, Senior Director, Investor Relations and Corporate Communications

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#### **Background Notes**

#### 1. BB-10901

BB-10901 is an immunoconjugate of the humanised monoclonal antibody, huN901, which binds to a particular protein found on the surface of certain tumour cells, and a powerful cytotoxic agent, DM1. Thus, it is designed to selectively seek out and kill certain types of cell, including those found in small cell lung cancer (SCLC) tumours. In pre-clinical studies, BB-10901 eradicated SCLC tumours. Under the same experimental conditions, other chemotherapies used to treat SCLC, such as cisplatin and etoposide produced only a temporary interruption of tumour growth. [Chari, R. V. J., et. al. Proceedings AACR, 2001, Abstract 4405; Liu, C., et.al. Proceedings AACR, 1997, Abstract 190]

Earlier this year, data from the ongoing U.S. Phase I study of BB-10901 were presented at the 2002 Annual Meeting of the American Society of Clinical Oncology (ASCO). The presentation included data on the product's pharmacokinetics and tolerability; initial evidence of biological activity was also presented. Patients in this study are now being dosed at 75 mg/m<sup>2</sup>.

#### 2. ImmunoGen, Inc.

ImmunoGen, Inc. develops innovative biopharmaceuticals for the treatment of cancer. The Company's Tumour-Activated Prodrug (TAP) technology couples highly potent cytotoxic agents with tumour-targeting antibodies to create effective new treatments for cancer with minimal damage to normal tissue. Two TAP products developed by ImmunoGen are in clinical trials – huN901-DM1/BB-10901 and cantuzumab mertansine; the latter is licensed to GlaxoSmithKline.

#### 3. British Biotech

British Biotech is a research and development stage pharmaceuticals company aiming to develop and commercialise specialist drugs for serious illnesses, principally cancer. It currently has four products in or near to patient trials, supplemented by focused drug discovery research programmes.

#### **Product Portfolio**

BB-10901 – A Tumour-Activated Prodrug product, currently in Phase I/II trials in small cell lung cancer. British Biotech acquired exclusive European and Japanese development and commercialisation rights to BB-10901 from ImmunoGen Inc. (Boston, USA) in May 2000.

MG98 – A 2nd generation antisense inhibitor of DNA methyltransferase (DNMT), a nuclear enzyme implicated in uncontrolled tumour growth. British Biotech acquired exclusive European development and commercialisation rights to MG98 from MethylGene Inc. (Montreal, Canada) in February 2002.

BB-10153 – A novel thrombolytic, about to start a Phase II proof-of-principle study in heart attack patients. The study will be conducted by the Thrombolysis in Myocardial Infarction Study Group, a US-based investigative team at the forefront of clinical research into acute coronary syndromes.

BB-83698 –A peptide deformylase inhibitor targeted at community-acquired pneumonia (hospitalised patients). In completed pre-clinical studies BB-83698 has shown high potency against a range of gram positive bacteria, including several drug-resistant strains. A Phase I clinical study in healthy volunteers, to determine the safety and pharmacokinetics of single doses of an intravenous formulation, is expected to begin in October 2002.

#### Research

Antibiotic Programme – A research programme into the use of inhibitors of peptide deformylase and other bacterial metalloenzymes to treat infectious disease. The programme has produced several lead compounds in research and pre-clinical development, with high potency shown against drug resistant gram-positive and gram-negative pathogens.

Anti-Inflammatory Programme – Working in collaboration with Serono SA, this research programme is investigating the use of metalloenzyme inhibitors as new treatments for serious inflammatory diseases, particularly multiple sclerosis.

Cancer Programme – As part of its collaboration with MethylGene on MG98 (see above) British Biotech has an exclusive option to European development and commercialisation rights for compounds from MethylGene's research into small molecule inhibitors of DNMT.

Biodefence Research – As part of the UK Government's biodefence initiative, the Defence, Science and Technology Laboratory (DSTL) of Porton Down is investigating the utility of selected British Biotech metalloenzyme inhibitors against anthrax lethal toxin and botulin toxin.

## **News Release**

### **British Biotech**

For release: 9 August 2002

### British Biotech and GeneSoft collaborate to discover and develop novel antibiotics

#### First in class product expected in clinic by Q4 2002

British Biotech plc (LSE: BBG, Nasdaq: BBIOY) and GeneSoft Inc. announced today that they have signed agreements for a broad-based collaboration to discover and develop novel anti-infective drugs based on British Biotech's proprietary bacterial metalloenzyme inhibitors.

Combining British Biotech's novel targets, chemistry and clinical development with GeneSoft's experience in antibiotic lead optimisation and clinical expertise, the collaboration will focus on three specific areas:

- clinical development and marketing of BB-83698, British Biotech's lead peptide deformylase (PDF) inhibitor, governed by a licence, development and commercialisation agreement;
- lead optimisation and clinical development of oral PDF inhibitors, governed by a research agreement; and
- drug discovery research exploiting British Biotech's portfolio of intellectual property and expertise in respect of other microbial metalloenzyme targets, governed by a research agreement.

GeneSoft will make an initial payment to British Biotech of US\$4 million. On commencement of a Phase I study of BB-83698, anticipated in October 2002, GeneSoft will pay British Biotech a further US\$1 million and equity representing 3.45 per cent of GeneSoft.

"GeneSoft is delighted to partner with British Biotech to discover and develop new antibiotics," said Gary Patou, MD, GeneSoft's President. "The medical community desperately needs new mechanism of action antibiotics to combat multidrug resistant bacteria. We believe that the programmes developed within British Biotech have tremendous potential to bring new antibiotics to patients."

Welcoming the agreement, British Biotech Chief Executive Dr Elliot Goldstein said: "Through this collaboration British Biotech has achieved its three key objectives of expanding the Antibiotic Programme, while sharing the costs and commercialisation rights. GeneSoft is an ideal partner for the programme. It specialises in antibiotic drug discovery and development and brings a wealth of clinical and scientific expertise in this field."

#### **BB-83698**

BB-83698 represents a new class of antibiotic and is targeted at hospitalised patients with community-acquired pneumonia. A Phase I clinical study in healthy volunteers, to determine safety and pharmacokinetics of single doses of an intravenous formulation, is expected to begin in October 2002.

Under the first part of the collaboration, British Biotech and GeneSoft have entered into an exclusive agreement to co-develop and commercialise BB-83698. The development costs will be shared equally by British Biotech and GeneSoft, as will the world-wide profits.

#### PDF research programme

In support of BB-83698, British Biotech and GeneSoft have entered into an exclusive research agreement, for an initial period of three years, to identify further PDF inhibitors for clinical development, including oral inhibitors for broader indications. The collaboration will allow increased resource and capabilities to be applied to the PDF programme to exploit fully the potential of this novel series of agents. British Biotech will maintain resources on this programme at current levels with GeneSoft adding resource equivalent to 170 per cent of British Biotech's. As with BB-83698, development costs and world-wide profits are shared equally.

#### Other metalloenzyme targets

GeneSoft will select from British Biotech's other anti-microbial metalloenzyme programmes, and determine the research projects that it wishes to progress. British Biotech will receive undisclosed milestone and royalty payments on the successful development and commercialisation of any products from each research project.

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#### Enquiries:

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This news release contains forward-looking statements that reflect the Company's current expectations regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the success of the Company's research strategies, the applicability of the discoveries made therein, the successful and timely completion of clinical studies and the uncertainties related to the regulatory process.

#### **Background Notes**

#### 1. The need for new antibiotics

One of the key contributors to morbidity and mortality due to bacterial infections is the increasing prevalence of drug-resistant bacteria. The combination of a limited number of targets, widespread use of prophylactic therapy, empirical treatment with broad-spectrum agents, and the natural evolution of bacteria, has contributed to a resurgence of antibiotic resistance and the creation of a major public health problem. New structural classes of antibiotics that target alternative, essential bacterial processes are likely to make significant inroads into the anti-infectives market.

Bacterial genomes contain a number of metalloenzymes, several of which are believed to be essential to survival, and bacterial polypeptide deformylase (PDF) is now widely recognised as an attractive target for antibacterial chemotherapy (Giglione *et al*, 2001 *Molecular Microbiology*, vol 36, 1197-205). Deformylation is a crucial step in bacterial protein biosynthesis and the PDF enzyme is essential for bacterial growth, with the gene encoding PDF (def) found to be present in all sequenced path'ogenic bacterial genomes.

In research and pre-clinical studies, British Biotech's PDF inhibitors have shown a microbiological activity profile suitable for respiratory tract pathogens and high potency against antibiotic-resistant organisms. BB-83698, the company's lead PDF inhibitor compound, has now completed the toxicology studies necessary to allow human dosing and a Phase I clinical study in healthy volunteers, to determine the safety and pharmacokinetics of single doses of an intravenous formulation, is expected to begin in October 2002.

#### 2. GeneSoft Inc

GeneSoft is a privately held biopharmaceutical company headquartered in South San Francisco, California. GeneSoft was founded in 1998 by Peter Dervan, Ph.D. and others based on proprietary chemistry technology licensed from the California Institute of Technology. GeneSoft has been using its proprietary technology to discover and develop novel anti-infective products, and currently has a portfolio of lead compounds in late pre-clinical studies. Since its founding, GeneSoft has raised over \$60 million in equity capital from investors in the United States, Europe and Asia.

For more information please visit www.genesoft.com

#### 3. British Biotech

British Biotech is a research and development stage pharmaceuticals company aiming to develop and commercialise specialist drugs for serious illnesses, principally cancer. It currently has four products in or near to patient trials, supplemented by focused, collaborative drug discovery research programmes.

#### **Product Portfolio**

BB-10901 – A Tumour-Activated Prodrug product, currently in Phase I/II trials in small cell lung cancer. British Biotech acquired exclusive European and Japanese development and commercialisation rights to BB-10901 from ImmunoGen Inc. (Boston, USA) in May 2000.

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BB-10153 – A novel thrombolytic, about to start a Phase II proof-of-principle study in heart attack patients. The study will be conducted by the Thrombolysis in Myocardial Infarction Study Group, a US-based investigative team at the forefront of clinical research into acute coronary syndromes.

BB-83698 –A peptide deformylase inhibitor targeted at community-acquired pneumonia (hospitalised patients). (See above.)

#### Research

Antibiotic Programme – Now working in collaboration with Genesoft, this research programme is focused on the development of bacterial metalloenzyme inhibitors as novel anti-infective drugs (see above).

Anti-Inflammatory Programme – In collaboration with Serono SA, this research programme is investigating the use of metalloenzyme inhibitors as new treatments for serious inflammatory diseases, particularly multiple sclerosis.

Cancer Programme – As part of the collaboration with MethylGene on MG98 (see above) British Biotech has an exclusive option to European development and commercialisation rights for compounds from MethylGene's research into small molecule inhibitors of DNMT.

Biodefence Research – As part of the UK Government's biodefence initiative, the Defence, Science and Technology Laboratory (DSTL) of Porton Down is investigating the utility of selected British Biotech metalloenzyme inhibitors against anthrax lethal toxin and botulin toxin.

### **British Biotech**

3<sup>rd</sup> July 2002

Company Announcements Office Stock Exchange London EC2N 1HP

Dear Sir,

Pursuant to the terms of remuneration agreed between British Biotech plc and its subsidiaries ("British Biotech") and its Chairman, Mr Chris Hampson, it is announced that Mr Hampson, on 3<sup>rd</sup> July 2002, acquired 39,533 ordinary shares in British Biotech at a price of 7.5p per share.

Following this purchase, Mr Hampson is interested in a total of 683,491 ordinary shares.

Yours faithfully

Sian Bishop Legal Counsel